REMARKS

The foregoing amendment cancels claims 42-47 and adds new claims 48 and 49. Pending in the application are claims 1-22, 24-41, 48 and 49, of which claims 1, 15, 48 and 49 are independent. The following comments address all stated grounds for rejection and place the presently pending claims, as identified above, in condition for allowance.

New independent claims 48 and 49 recite the subject matter of claims 1 and 15, respectively, and further specify that the fluid interface ports are substantially disk-shaped, as set forth in the specification and shown in the Figures. *No new matter is added.*

Amendment and/or cancellation of the claims is not to be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicant reserves the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

Double Patenting Rejection

Claims 1-22 and 24-41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 and 58-150 of copending Application No. 10/028,852 as characterized by US 2003/0007898 and claims 1-45 copending Application No. 10/057,354. Applicants submit that the claims are patentably distinct from the claims of co-pending U.S. Patent Application Nos. 10/028,852 and 10/057,354.

In addition, the Examiner rejects claims 1-22 and 24-41 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent Number 6,877,528. The claims in the present application are entirely different from the claims in U.S. Patent Number 6,877,528. For example, the claims in the present invention are directed to a fluid interface port for interfacing fluid between an interior and an exterior of a channel. In contrast, the claims of the '528 patent are directed to a valve for a microfluidic device for regulating fluid flow therein. The meniscus in the '528 claims interfaces a side channel with a reservoir, not an exterior environment, that is used to create a pressure pulse. In contrast, the meniscus in the present application is formed within and co-planar with a side wall of a channel,

such that the meniscus is flush with the side wall. In addition, the meniscus in the claims of the '528 patent is not necessarily a virtual wall and used only to transfer a pressure pulse to a flow channel in order to regulate flow therein. The meniscii in the two sets of claims have different configurations and purposes. In addition, both the claims of the '528 patent recite different features, such as a gas-filled first reservoir, a buffer reservoir, actuators, side channels not present in the claims of the present invention.

Claim Rejections Under 35 USC §112

Regarding the rejection of claims 1-22 and 24-41 under 35 USC §112, Applicants submit that the cited recitation is clear and definite. The recitation specifying that the diameter of the fluid interface port is significantly larger than the depth of the fluid interface port should be given patentable weight, because the structural recitation is clear and definite. The recitation requires that the depth of the fluid interface port be significantly smaller than the diameter, which is between about 25 microns and about 100 microns. Therefore, the depth depends on where the diameter falls within this range, but the depth must be substantially smaller than the diameter. Because the diameter of the port is significantly larger than the depth of the port, the port therefore has substantially a disk shape. Applicants submit that the relationship between the dimensions of the depth and diameter is clear and definite and that the overall dimensions of the depth and diameter are also clear and definite, and request reconsideration of the rejection under 35 USC §112.

Claim Rejections Under 35 USC §102

In the Office Action, the Examiner rejects claims 1-22 and 24-41 under 35 U.S.C. 102(e) as being anticipated by the Chow reference (U.S. Patent Number 6,494,230), claims 1-22 and 24-41 under 35 U.S.C. 102(b) as being anticipated by the Handique reference (U.S. Patent Number 6,130,098), and claims 1-22 and 24-41 under 35 U.S.C. 102(b) as being anticipated by the Fuchs reference (U.S. Patent Number 5,757,482). Applicants submit that the pending claims distinguish patentably over the cited references, and request reconsideration and allowance of the pending claims.

Applicants maintain that the cited references, alone or in combination, do not disclose a device having a fluid interface port with a diameter that is substantially greater than the depth of the fluid interface port, as recited in independent claims 1 and 15. The recited fluid interface ports thus have has a *disk* shape, as shown in Figures 2A and 2B, and described on page 17, lines 19-20, to facilitate *direct* access to the channel interior, a feature not taught or suggested in the cited references.

The cited references also fail to disclose a device including a fluid interface ports having a dead volume of less than about one *nanoliter*, formed in the side wall of a channel having a virtual wall formed by a separation medium disposed in the interior of the separation channel, and which each virtual wall having a meniscus surface that is substantially co-planar with the side wall channel in which the virtual wall is formed, as recited in independent claims 1 and 15. In fact, Applicants submit that the cited references teach *away* from the claimed invention.

Applicants respectfully submit that the recitation "co-planar" is intended to specify that the meniscus formed in the fluid interface port aligns with the side wall and is the same thickness as the wall, such that the meniscus, not the liquid in the channel, essentially replaces the removed portion of the side wall creating the fluid interface port. The top of the meniscus aligns with the top, outer end of the side wall, while the bottom aligns with the lower, inner end of the wall, and the meniscus fills the opening in the wall. Because the volume of the meniscus is measured based on the bottom edge of the meniscus, which aligns with the bottom edge of the opening at the inner side of the side wall, the dead volume of the fluid within the actual opening is significantly minimized, and preferably zero.

The ability to form a virtual wall that consists of a meniscus that is co-planar with a side wall in which the meniscus is formed requires precise, particular and difficult calculation, design, measurement and engineering, and is significantly lacking in the prior art.

The particular configuration of the claimed fluid interface port facilitates a low dead volume, or a zero dead volume, rather than the particular characteristics of the fluid and pressure in the system.

In contrast to the claimed configuration, the passage 310 of Chow, which the Examiner considers to be a fluid interface port, comprises a channel having a depth that is significantly *larger* than the cross-section of the channel, which prevents direct interfacing of the channel interior with the ambient. The passage 310 of Chow is also incapable of forming a meniscus that is co-planar with a side wall of a channel. Rather, because the depth of the passage 310 is relatively large, the meniscus is formed only within a portion of the passage and cannot be positioned co-planar to the side wall.

In addition, the vent 70 in Handique, which the Examiner considers to be a fluid interface port, also forms a channel having a depth that is significantly *larger* than the cross-section of the channel, in contrast to the claimed invention. The vent 70 is also incapable of positioning a meniscus in a co-planar location with a side wall. Rather, any meniscus formed in the vent 70 of Handique will align only with a small portion of a side wall, in contrast to the claimed invention.

The Fuchs reference also does not disclose the claimed invention. As shown in Figure 4, the cross-sectional diameter of the port 24 in Fuchs is significantly *larger* than the channels 12. In addition, the Fuchs reference discloses that the port 24 is formed in the cover 12, which is at least 400 microns thick, as set forth in column 5, lines 12-14. Therefore, even *if* the diameter of the port 24 were significantly larger than the depth, as recited in claims 1 and 15, the diameter would be required to be several times the recited range of between about 25 μm and about 100 μm, precluding formation of a virtual wall, specifically a virtual wall with minimal dead volume. In clear contrast to the claimed invention, the port 24 in Fuchs is *large*, does not form a meniscus, or a meniscus capable of forming a virtual wall, does not minimize dead volume, and does not form a *direct* interface between a channel interior and an external environment. In addition, even if a meniscus were formed in the port 24 of Fuchs, the meniscus would not be co-planar with a side wall, as set forth in claims 1 and 15.

In addition, independent claims 1 and 15 further distinguish over the cited references, because the references fail to disclose a fluid interface port forming a virtual wall having a meniscus surface that is co-planar with a side wall in which it is formed. Even if a meniscus were formed in the channel 301 of Chow, the vent 70 of Handique and/or the port 24 of Fuchs, such a meniscus would only be formed in a top portion of the channel and would not align with the side wall in which the channel is formed, as recited in claims 1 and 15.

Furthermore, none of the cited references disclose a fluid interface port capable of forming a *virtual wall*. The virtual wall forms a *direct* interface between the microchannel interior and the microchannel exterior, allowing direct access to the liquid in microchannel without introducing dead or unswept volume in the microchannel. Even if the devices in the cited references were capable of forming menisci, the menisci would not form *virtual walls*.

As used in the present application, a "virtual wall" is not an interconnecting channel or simply an opening to a channel. Rather, a virtual wall refers to a particular type of *meniscus* formed in an opening of a side wall of a microchannel that is sized and dimensioned so that the meniscus essentially replaces the removed portion of the side wall that defines the fluid interface port. A virtual wall does not refer to *any* and every type of meniscus (i.e., all menisci are not virtual walls), but rather a meniscus in an opening that is specifically sized and configured so that the fluid flow through the microchannel is not affected by the fact that a portion of the side wall of the microchannel is absent and that the microchannel is exposed to the environment (see the specification at page 17, lines 10-30). The term "virtual wall" is used to denote that the meniscus formed by a fluid in the fluid interface port essentially replaces the removed portion of the side wall that forms the port. The word 'virtual' in the present claims refers to the effect that the overall liquid flow through the separation channel of the electrophoretic system is not influenced by the virtual wall, i.e. the flow of liquid in the micro-plate having a virtual wall is substantially identical to the flow of liquid through an identical micro-plate in which no virtual wall is formed.

The virtual wall forms a *direct* interface between the microchannel interior and the microchannel exterior, allowing direct access to the liquid in microchannel without introducing dead or unswept volume in the microchannel. In contrast, channel 301 in the Chow reference does not *directly* interface a microchannel to the environment surrounding the device. In addition, the vent 70 in Handique also does not form a direct interface, but rather a long, indirect opening with a large dead volume.

The virtual wall of the claimed invention also serves to seal liquid inside of the microchannel through a range of pressures in the microchannel. There is no teaching or

suggestion that liquid is sealed in the device by the channel 310 of Chow, the vent 70 of Handique or the port 24 of Fuchs.

A fluid interface port forming a virtual wall according to the present invention generally has a diameter between about 25 μm and about 125 μm such that resulting capillary forces retain liquid within the microchannel. There is no teaching or suggestion that the channel 301 of Chow, the vent 70 of Handique and the port 24 of Fuchs have such dimensions.

As set forth in independent claims 1 and 15, a virtual wall also has a relatively low dead volume, i.e., less than about one nanoliter. As set forth in the specification, "dead volume" refers to the volume of liquid retained in a fluid interface port (i.e. the volume of liquid the fluid interface port holds that is not flushed through the fluid interface port by the flow field of the first liquid through the microchannel). The relatively small dead volume provided by the virtual wall results in a direct fluid interface allowing direct injection of a precise volume of sample into the interior of the microchannel from the exterior of the microchannel. The ability to directly inject sample into the microchannel due to the low dead volume of the fluid interface port provides improved control over the amount of sample that is injected into the microchannel, allows efficient use of sample, and significantly reduces waste of the sample. Furthermore, the direct injection provided by the very small dead volume reduces or prevents cross-contamination between different samples and allows a second substance to be directly injected into the system immediately after a first substance without requiring flushing of the fluid interface port. In contrast, the channel 301 of Chow, the vent 70 of Handique and the port 24 of Fuchs have large dead volumes.

The larger dead volumes in the cited references may lead to dispersion of the sample, a time delay between the time of injection and the time when the sample enters the microchannel, injection inefficiency, potential cross-contamination between different samples and difficulty controlling the amount of sample that actually reaches the microchannel. These problems are avoided or reduced by the use of the fluid interface port forming a virtual wall having a dead volume of less than about one picoliter according to the illustrative embodiment.

For at least these reasons, claims 1 and 15, and dependent claims 2-14, 16-22 and 24-41 distinguish patentably over the cited references.

NEW CLAIMS

New claim 49 recites the subject matter of claim 1 and further specifies that the fluid interface port is disk-shaped. New claim 48 recites the subject matter of claim 15 and further specifies that the fluid interface port is disk-shaped. The new claims are patentable for the same reasons claims 1 and 15 are patentable, as described above. In addition, the specific recitation that the fluid interface port is disk-shaped is patentable.

For at least these reasons, Applicants respectfully submit that all pending examined claims are patentable, and request that the objections and rejections be reconsidered and withdrawn.

CONCLUSION

In view of the above amendment, applicants believe the pending application is in condition for allowance.

Applicants believe no fee is due with this Amendment. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. TGZ-001C from which the undersigned is authorized to draw.

Dated: August 30, 2006

Respectfully submitted,

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